Queen's University Belfast

Research and Enterprise

Standard Operating Procedure
Research Governance

Title:	**Preparation, Completion, Signing and Correcting Case Report Forms**		
SOP Reference Number:	QUB-ADRE-007	Date prepared	17 July 2008
Version Number:	Final v 5.0	Revision Date	15 September 2016
Effective Date:	01 October 2016	Review Date:	August 2018

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Revision Log

Previous Version number	Date of Review/Modification	Reason for Review/Modification	New Version Number
Final v 1.0	10/11/09	Annual Review	Final v 1.0
Final v 1.0	10/11/10	Annual Review/ Update following MHRA GCP Inspection	Final v 2.0
Final v 2.0	20/08/2012	Periodic Review	Final v 3.0
Final v 3.0	21/10/2014	Periodic Review	Final v 4.0
Final v 4.0	15/09/2016	Periodic Review	Final v 5.0

1. Purpose

This Standard Operating Procedure (SOP) is to describe the procedure for completing, signing and correcting Case Report Forms (CRFs).

This SOP has been prepared with Investigational Medical Product (IMP) studies in mind, but it should be used for other studies, as appropriate.

2. Introduction

ICH Good Clinical Practice Guidelines define a Case Report Form (CRF) as *"A printed, optical or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject".*

CRFs are the official documentation of the trial for the Sponsor, Regulatory Authorities (such as the Medicines and Healthcare products Regulatory Agency (MHRA) and in the case of multi-centre trials, the investigator sites. In the event of an audit or inspection, CRFs, in conjunction with source documents (e.g. health records) will be subject to examination.

The data collected on the CRF will form the basis of the trial report, any publications and, in the event of an Investigational Medicinal Product (IMP) study, contribute to the data required for regulatory approval of a new drug license or indication of same. Therefore, it is necessary to ensure that CRFs are legible, accurate, complete, authentic and prepared in a timely fashion.

A well-designed CRF acts as a reminder to investigators and ensures that the protocol is being followed.

3. Scope

This SOP applies to all studies where the University is acting in the capacity of Sponsor, or Co-Sponsor. It applies to all members of University staff; both academic and support staff as defined by Statute 1, including honorary staff and students. The University does not sole sponsor CTIMPs and therefore, the Lead Sponsor's requirements and approval of CRFs should always be met.

4. Responsibilities

The Chief Investigator (CI) is ultimately responsible for ensuring that data entered into the CRF is correct and complete.

Responsibility can be delegated in accordance with the SOP on Delegated Responsibility QUB-ADRE-005 to other investigators involved in the research for the set up, completion and recording of CRFs.

5. Procedure

5.1 Preparation - General

Each page of the CRF should have the following information as a header:

- Name of study or study number;
- Patient Code Number;
- Patient Initials;
- Date in the format of dd/mm/yyyy to capture the clinical visit/information.

Each page of the CRF should have the following information as a footer:

- Signature of the delegated individual completing the page;
- Signature of the CI with responsibility of signing off the entry;
- If the CRF extends over a number of pages indicate on each the number of the page in conjunction with the length of the document i.e. page 1 of 3, page 2 of 3, page 3 of 3.

There should be a logical layout to the CRF that is consistent with the protocol and follows the schedule of clinic visits.

The CI should collaborate with the statistician when developing the CRF and ensure that all those involved in the research study have a clear understanding of the contents of the CRF, before it is signed off.

The number of pages in the CRF will be dependent upon the nature of the study. Pages which include laboratory results should have the units of measurement pre-printed alongside each entry.

To facilitate data collection and subsequent analysis:
- Provide choices for each question;
- Collect raw data rather than calculated data;
- Ensure that a standard approach is taken to answering the questions i.e. answers are to be circled, underlined, deleted or a box ticked. The ticking of a box provides for less confusion.

5.2 Preparation - Specific

The following examples are not meant to be an exhaustive list but are to provide some guidance as to what should be contained in a CRF. The common contents are:

- Demographic information:
  (i) Gender;
  (ii) Date of Birth;
  (iii) Date of Visit.

- Inclusion / Exclusion Criteria giving tick boxes to demonstrate compliance with each criterion.

- Screening pages:
  (i) Medical examination;
  (ii) Vital signs;
  (iii) Laboratory results;
  (iv) Other tests required to demonstrate compliance with the inclusion criteria;
  (v) Concomitant medication.

- Visit pages:
  (i) Vital signs to be measured at each visit;
  (ii) Record of any procedure to be carried out;
  (iii) Laboratory results;
  (iv) Adverse event from for each visit;
  (v) Any changes to concomitant medication.

- Early termination / withdrawal of participation page that includes:
  (i) The date of termination / withdrawal;
  (ii) A checklist giving information on the reason(s) for early termination / withdrawal.

- An end of study page that includes the date of study completion (dd/mm/yyyy).

5.3 Completion of CRFs

All CRFs are to be completed in accordance with GCP guidelines and as soon as possible after each clinical trial visit.

Entries should be:

- In English;
- Legible;
- In permanent ink, preferably black ballpoint pen;
- Verifiable.
- The confidentiality of the research participant must be maintained at all times. The research participant must only be identified in the CRF using a trial number or code. Only where the protocol specifies that CRFs are source documents and that the patient name can be collected, should names appear. In addition, informed consent must be obtained to retain patient identifiable information on University premises as outlined in QUB-ADRE-004.
- Data should be complete with no fields left blank. If data are unavailable it is necessary to write 'not applicable', 'missing', 'not known' or 'test not done' on the CRF.
- Likewise, do not create additional fields. Only provide the information that is asked for.
- All CRF data derived from source documents must be accurately transcribed, in particular, when copying out results, such as laboratory results. Any discrepancies with source data should be explained and the significance noted in the CRF and the source document.
- Unless otherwise agreed, laboratory values should be entered without conversion from printed reports. If conversions are required, in the case of multicentre studies where units of measurements may differ, space should be made in the CRF for the original figure, the conversion factor and the converted result. This facilitates the checking of calculations by trial monitors and regulatory authorities.

5.3.1 Correcting

Corrections should be made by crossing through the incorrect entry with a single line so that the original entry is still readable. Do not use correction fluid, completely obliterate the entries or overwrite an entry. The correct data should then be entered, the correction dated and initialled and if necessary an explanation given of the correction.

5.3.2 Signing

When all entries and corrections are deemed to be complete, the CRF must be signed by the CI (or designee) to assert that they believe it to be complete and correct.

Before any monitoring visit, the relevant members of the research team should ensure that all CRFs are as up to date as possible.

5.3.3 Storing and Access

CRFs should be stored in secure storage cabinets and a secure location during the course of the study. They must be archived when the study has finished. The Standard Operating Procedure for the setting up, maintaining and archiving of trial master file(s)/site master file(s) QUB-ADRE-008 should be complied with. Therefore, CRFs should be retained with the Study Master File and centrally archived.
Access to CRFs should be restricted to the Investigators, study monitors and Regulatory Authorities.

6 References

International Conference on Harmonisation (ICH) Harmonisation Tripartite Guideline: Guideline for Good Clinical Practice EB (R1). (Last accessed September 2016) http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf

Imperial College London, SOP Reference CRO/SOP/007 Case Report Forms.